Complete Summary

GUIDELINE TITLE

Laboratory guidelines for screening, diagnosis, and monitoring of hepatic injury.

BIBLIOGRAPHIC SOURCE(S)

Dufour DR, Lott JA, Nolte FS, Gretch DR, Koff RS, Seeff LB. Diagnosis and monitoring of hepatic injury. I. Performance characteristics of laboratory tests. Clin Chem 2000 Dec;46(12):2027-49. [266 references]

Dufour DR, Lott JA, Nolte FS, Gretch DR, Koff RS, Seeff LB. Diagnosis and monitoring of hepatic injury. II. Recommendations for use of laboratory tests in screening, diagnosis, and monitoring. Clin Chem 2000 Dec;46(12):2050-68. [220 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hepatic injury

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Screening

CLINICAL SPECIALTY

Family Practice
Gastroenterology

Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pathology
Pediatrics

INTENDED USERS

Clinical Laboratory Personnel
Physicians

GUIDELINE OBJECTIVE(S)

- To provide information on performance characteristics for tests that are commonly used to identify acute and chronic hepatic injury
- To provide guidelines on the use of laboratory tests in screening, diagnosis, and monitoring of acute and chronic hepatic injury

TARGET POPULATION

Patients with hepatic injury

INTERVENTIONS AND PRACTICES CONSIDERED

Screening/Diagnosis/Monitoring (see "Major Recommendations" field for context)

1. Liver Function Tests
    - Aminotransferases (AST, ALT)
    - Alkaline phosphatase (ALP)
    - Gamma-glutamyltransferase (GGT)
    - Bilirubin
    - Albumin
    - Prothrombin time (PT)
2. Hepatitis Serologic and Nucleic Acid Tests

    Hepatitis A virus (HAV)

    - Anti-HAV immunoglobulin M (IgM)
    - Total antibody

    Hepatitis B virus (HBV)

    - Hepatitis B virus surface antigen (HBsAg)
    - Antibody to hepatitis B virus surface antigen (anti-HBs)
    - IgM antibody to hepatitis B virus core antigen (anti-HBc)
    - Total anti-HBc
    - Hepatitis B virus e antigen (HBeAg)
    - Antibody to HBeAg antigen (anti-HBe)

    Hepatitis C virus (HCV)

- HAV and HBV markers
- Anti-HCV
- HCV RNA
- HCV RIBA

Hepatitis D virus (HDV)

- HBsAg
- IgM anti-HBc
- Total anti-HDV

Hepatitis E virus (HEV)

- ORF2 antigen

3. Other Laboratory Tests
   - Anti-nuclear antibodies (ANA)
   - Anti-smooth muscle antibodies
   - Ceruloplasmin
   - Alpha1-antitrypsin (A1AT)
   - Liver biopsy
   - Alpha-fetoprotein (AFP)
   - Iron, iron binding capacity, ferritin, HFE gene mutation

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Part I. Performance Characteristics of Laboratory Tests

A comprehensive literature search was conducted of English-language articles in Index Medicus from 1966 to 1998, with "Knowledge Finder" as a search engine. Key search words included hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (HDV), hepatitis E (HEV), hepatitis G, TT virus, alcoholic hepatitis, alpha1-antitrypsin, Wilson´s disease, hemochromatosis, autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, cirrhosis, hepatocellular carcinoma, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT), bilirubin, ammonia, and laboratory analytical performance goals. Compound searches were performed using the terms "fibrosis markers and chronic hepatitis", "HCV and genotype", and "prothrombin time (PT) and liver disease". For several of the key words, the search was repeated in August 1999 for articles from 1998 and 1999. The filter was set for fuzzy logic for word matching and to select the top 1000

matches in order of relevance. All titles with high or moderate relevance values were reviewed, and if they appeared to address the topics selected, the abstracts were reviewed to select articles for further study. A total of >750 articles were selected for review; additional references were selected from the bibliographies of the articles selected.

Part II. Laboratory Tests in Screening, Diagnosis, and Monitoring

A MEDLINE search was performed for key words related to hepatic diseases, including acute hepatitis, chronic hepatitis, alcoholic hepatitis, cirrhosis, hepatocellular carcinoma, and etiologic causes. Abstracts were reviewed, and articles discussing use of laboratory tests selected for review. Additional articles were selected from the references.

NUMBER OF SOURCE DOCUMENTS

Part I. Performance Characteristics of Laboratory Tests: More than 750 articles

Part II. Laboratory Tests in Screening, Diagnosis, and Monitoring: Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The Practice Guidelines Committee of AASLD adopted modified categories of the Quality Standards of the Infectious Diseases Society of America. These categories are reported with each recommendation, using the Roman numerals I-IV to determine quality of evidence on which recommendations are based.

Quality of Evidence

I. Evidence from multiple well-designed randomized controlled clinical trials, each involving a number of patients to be of sufficient statistical power
II. Evidence from at least one large well-designed clinical trial with or without randomization, from cohort or case-controlled analytical studies, or well-designed meta-analysis
III. Evidence based on clinical experience, descriptive studies, or reports of expert committees
IV. Not rated

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guideline represents a consensus of both (the National Academy of Clinical Biochemistry and the American Association for the Study of Liver Diseases) guideline committees.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of the Recommendation

A. Survival benefit
B. Improved diagnosis
C. Improvement in quality of life
D. Relevant pathophysiologic parameters improved
E. Impacts cost of healthcare

COST ANALYSIS

General screening of the population for chronic hepatic injury is not cost-effective and should be limited to high-risk individuals.

A decision analysis on published reports of screening for hepatocellular carcinoma (HCC) in Western patients with compensated cirrhosis concluded that, for patients with a likelihood of survival of 85% at 5 years, screening would likely add 3–9 months to average life expectancy at a cost of $26 000 to $55 000 per year of life gained, figures that compare favorably to those for colon cancer and breast cancer screening.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were reviewed in a multistep process. An initial draft was prepared by the committee and reviewed by 11 experts: 8 in the field of hepatology, and 3 in laboratory medicine. On the basis of the comments received, a second draft of the guidelines was prepared and presented to the American Association for the Study of Liver Diseases (AASLD) Practice Guidelines Committee and NACB board of directors. A third draft was then prepared and posted on the NACB website for open comments, and presented in a 2-day, NACB-sponsored symposium at the AACC Annual Meeting in July 1999. A transcript of the comments made at the symposium was reviewed by the committee, and modifications to the guidelines were again presented to the AASLD Practice Guidelines Committee and the NACB board of directors for final comments. The guidelines were then reviewed and

approved by the AASLD Council. These guidelines represent the product of the final modifications based on those comments.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the level of the quality of the evidence (Level I-Level IV) and the strength of the recommendation (A, B, C, D, E). Definitions of these ratings are presented at the end of the Major Recommendations field. Because of the nature of the guidelines, only categories B and E are used in the recommendations.

The following serum tests should be used to evaluate patients with known or suspected liver disease: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, direct bilirubin, total protein, and albumin (IIIB, E).

Performance Characteristics of Laboratory Tests

Aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT])

- Assays for alanine aminotransferase (ALT) activity should have total analytical error of ≤10% at the upper reference limit (IIIB). Current published performance goals for aspartate aminotransferase (AST), with total error of 15-20%, are adequate for clinical use (IIIB).
- Standardization of ALT values between methods and across laboratories is a priority need for patient care. Until standardization is accomplished, use of normalized results should be considered (IIIB).
- At a minimum, laboratories should have separate upper reference limits for adult males and females; reference limits should also be established for children and adults over age 60 by cooperative efforts (IIB).
- Unexpectedly increased ALT and/or AST should be evaluated by repeat testing; in individuals engaging in strenuous exercise, it should be repeated after a period of abstinence from exercise. Research is needed to determine the appropriate time interval required (IIIB and IIIE).

Alkaline Phosphatase (ALP)

- Assays for ALP activity should have total analytical error of ≤10-15% at the upper reference limit (IIIB).
- Separate reference limits should be provided for children, based on age and gender, and for pregnant women. A single reference interval is adequate for adults over age 25 (IIB).
- Specimens for ALP activity should be obtained in the fasting state; if not, mildly increased patient values should be reevaluated in the fasting state before further evaluation (IIB and IIE).
- Assays for ALP isoenzymes or measurement of other associated enzymes (such as gamma-glutamyl transferase [GGT]) are needed only when the source is not obvious from clinical and laboratory features (IIIB and IIIE).

Gamma-Glutamyl Transferase (GGT)

- Assays for glutamyltransferase activity should have total analytical error of ≤20% at the upper reference limit (IIIB).
- Use of fasting morning specimens is recommended (IIB).
- Although a single upper reference limit is appropriate for adult men, separate reference limits (based on age) are needed for children and adult women (IIB).
- Because of lack of specificity, GGT should be reserved for specific indications such as determining the source of an increased alkaline phosphatase (IIIB and IIIE).

Bilirubin

- Assays for total bilirubin should have a total analytical error of ≤20% (or 6.8 micromoles/L [0.4 mg/dL]) at the upper reference limit (IIIB).
- Separate upper reference limits should be used for total bilirubin in men and women. Although total bilirubin upper reference limits decline with age in adults, there is little significance to slight increases in bilirubin, and separate adult age-adjusted upper reference limits are not needed. In children, separate reference intervals should be used (IIIB).
- There are no data on analytical performance goals for direct or conjugated bilirubin. Laboratories should assure that direct bilirubin measurements are <1.7 micromoles/L (0.1 mg/dL) in most healthy individuals. Additional data are needed on performance goals in patients with increased conjugated bilirubin (IIIB).

Albumin

- Total error of <10% at the lower reference limit is adequate for clinical purposes; performance goals based on biological variation, although an ideal goal for measurement, cannot be met by most laboratories (IIIB).
- Assays for albumin in patients with liver disease should use bromcresol green. Bromcresol purple and electrophoresis determinations of albumin may be inaccurate in patients with liver disease (IIB).

Prothrombin Time (PT)

- PT in seconds rather than the international normalized ratio (INR) should be used to express results of PT in patients with liver disease (IIIB); however, this does not standardize results between laboratories (IIB).
- Additional research into standardization of reagents and use of derived indices (percentage of activity, INR) in liver disease is needed (IVB).

Ammonia

- Measurement of plasma ammonia (NH_3) for diagnosis or monitoring of hepatic encephalopathy is not routinely recommended in patients with acute or chronic liver disease; it may be useful in patients with encephalopathy of uncertain etiology (IIIB).
- Ideally, arterial, rather than venous, specimens should be used (IIB).

- Plasma should be separated from cells within 15 min of collection to prevent artifactual increases in ammonia (IIB).

Hepatitis Serologic Markers and Nucleic Acid Testing

Hepatitis A Virus (HAV)

- Anti-HAV immunoglobulin M (IgM) should be used to diagnose acute HAV infection (IB); HAV RNA tests are needed only for research purposes (IIIB).
- Total antibody should be used for determining immune status for HAV (IB).

Hepatitis B Virus (HBV)

- Tests for hepatitis B surface antigen (HBsAg), anti-hepatitis B surface antigen (anti-HBs), and anti-hepatitis B virus core antigen (anti-HBc) should be performed for diagnosis of current or past HBV infection. In suspected acute HBV infection, tests for IgM anti-HBc should be utilized (IB).
- Hepatitis B e antigen (HBeAg) and anti-HBeAg antigen (anti-HBe) should be measured only when indicated based on results of the initial tests (IIIB and IIIE).
- In patients with discordant results, tests should be repeated; persistently discordant results should be evaluated by a hepatologist or gastroenterologist (IIIB).
- Quantitative HBV DNA, HBeAg, and anti-HBe measurements should be used for monitoring response to antiviral therapy (IB).
- An international standard for HBV DNA tests should be established and manufacturers should calibrate methods against it (IIIB).
- Tests for HBV DNA should be quantitative, and the clinically useful dynamic range for HBV DNA tests should be defined (IIIB).

Hepatitis C Virus (HCV)

- Enzyme immunoassay (EIA) screening tests for HCV antibody are adequate for diagnosis of past or current HCV infection in a patient population with a high prevalence of disease; supplemental testing is not needed in such patients. If confirmation of active infection is required, HCV RNA should be used (IIB and IIE).
- Supplemental anti-HCV tests (recombinant immunoblot assay [RIBAs]) should be used in populations with low prevalence of disease or to confirm prior infection by HCV in a patient who is HCV RNA negative (IIIB and IIIE).
- Improved intermethod agreement and precision are needed for HCV RNA tests; methods should use a standard such as that developed by the World Health Organization (WHO) (IIB).
- Specimens for HCV RNA should be collected either as EDTA or citrated plasma or be centrifuged promptly to prevent falsely low results (IIB).
- Assays for HCV RNA should ideally have a dynamic range from <1000 copies/mL to >3.2 x 10^6 copies/mL (IIB).
- Genotype assays should reliably differentiate all six major genotypes and distinguish genotype 1a from 1b (IIIB and IIIE).

Hepatitis E Virus (HEV)

Assays for HEV antibodies should detect antibodies to the ORF2 antigen to assure adequate clinical specificity (IIIB and IIIE).

Recommendations for Use of Laboratory Tests in Screening, Diagnosis, and Monitoring

Acute Hepatic Injury

Acute hepatic injury can be diagnosed by ALT >10 times the upper reference limits and ALP <3 times the appropriate upper reference limit (IIB).

Markers of Severity

- Total bilirubin >257 micromoles/L (15 mg/dL) or PT >4 seconds above the upper reference limit in an individual with viral hepatitis, in the absence of other factors affecting results, indicates severe liver injury (IIB).
- Direct bilirubin is needed to rule out other causes of increased total bilirubin, such as hemolysis, but it does not differentiate hepatic injury from obstructive jaundice (IIB).
- With acetaminophen toxicity, a persistent increase in or increasing PT >4 days after ingestion indicates severe liver injury (IIB).

Differential Diagnosis

- Initial evaluation of acute hepatic injury should include a detailed drug history and viral markers (IgM anti-HAV, IgM anti-HBc, HBsAg, and anti-HCV) (IIB).
- Because of the need for postexposure prophylaxis, turnaround time of IgM anti-HAV should be <48 hours (IIIB and IIIE).
- If cost-effective (based on prevalence), laboratories may use total antibody to HAV and anti-HBc initially, performing IgM antibodies only if one or both is positive, if the turnaround time needs can be met (IIIE).
- Diagnosis of acute HCV infection (in a patient with a clinical picture of acute hepatic injury) can be presumptively made by negative HAV and HBV markers, recent exposure, and either negative anti-HCV and positive HCV RNA or negative anti-HCV at initial presentation with development of positive anti-HCV within 1-3 months (IIIB).
- Testing for HDV should be limited to patients with positive HBsAg, atypical clinical course, and high risk for HDV infection (IIB and IIE).

Other Causes

- In patients with negative viral markers and initial AST >100 times the upper reference limit, toxic exposure or ischemia should be suspected (IIB).
- In patients with negative viral markers and enzyme concentrations 8-100 times the upper reference limit, testing must exclude the possibility of Wilson disease and autoimmune hepatitis (AIH) (IIB).
- Testing for antibody to hepatitis E is not recommended in the United States unless other viral serologies are negative and there is a history of recent travel to an endemic area (IIIE).

- Tests for other infectious agents (Epstein-Barr virus [EBV], cytomegalovirus [CMV], syphilis, toxoplasmosis) may be used if no other causes are evident (IIB).

Monitoring

- PT >4 seconds above reference limits, bilirubin >257 micromoles/L (15 mg/dL), or development of encephalopathy identifies high-risk patients who require close monitoring and consideration of referral to a gastroenterologist or hepatologist (IIB).
- In patients with acute hepatitis B, repeat HBsAg measurements should be performed within 6-12 months; if negative and tests for anti-HBV surface antigen antibody (anti-HBs) are positive, no additional follow-up is needed (IIE).
- In patients with acute hepatitis C, ALT should be measured periodically over the next 1-2 years to assure continued normal results (IIB).

Chronic Hepatic Injury

- In the absence of liver biopsy showing chronic hepatitis, one of the following clinical definitions should be used to diagnose chronic hepatitis:

  Persistence of increased ALT for >6 months after an episode of acute hepatitis

  OR

  Increased ALT (without another explanation) on more than one occasion over a period of 6 months. A shorter time may be appropriate in patients with risk factors for chronic viral hepatitis, genetic causes of hepatic injury, or autoimmune liver injury, or in the presence of clinical signs or symptoms of liver disease (IIB).

Screening

- Screening for chronic hepatitis is recommended in asymptomatic high-risk individuals (IIB and IIE).
- ALT is the most cost-effective screening test for metabolic or drug-induced liver injury; AST should also be measured with history of alcohol abuse (IIB and IIE).
- Specific viral serologies (HBsAg and anti-HCV), as well as ALT, should be used in individuals at high risk for viral hepatitis (IB).
- Confirmation of chronic HCV infection in an anti-HCV-positive individual should be made by HCV RNA tests; if negative and ALT is increased, HCV RNA should be repeated (IIB).

Differential Diagnosis

- Initial evaluation should include a detailed drug history along with measurement of HBsAg and anti-HCV. If anti-HCV is positive, chronic infection should be confirmed by qualitative HCV RNA measurement (IIB and IIE).

- With persistently increased ALT and negative viral markers, the workup should include anti-nuclear antibodies (ANAs) and iron and iron-binding capacity (or unsaturated iron-binding capacity) (IIIB).
- In patients under age 40, ceruloplasmin should also be measured (IIIB).
- In patients negative for these markers, alpha1-antitrypsin (A1AT) phenotype may be of use (IIIB).
- If these tests are negative or inconclusive, diagnostic liver biopsy should be performed (IIIB).

Workup of Patients Without Obvious Cause for Chronic Hepatic Injury

Nonalcoholic Steatohepatitis (NASH)

Biopsy is necessary to establish the diagnosis of nonalcoholic steatohepatitis (IIB).

Hemochromatosis

- Initial evaluation for hemochromatosis should be by fasting serum transferrin saturation or unsaturated iron-binding capacity (IIB).
- Transferrin saturation $\geq$45% or unsaturated iron-binding capacity $\leq$28 micromoles/L (155 micrograms/dL) should be followed by analysis for HFE gene mutations (IIB).
- Screening of the population may be beneficial but is not currently recommended pending clarification of screening benefits (IIB and IIE).

Wilson's Disease

- Testing for Wilson's disease with ceruloplasmin is indicated in patients under age 40 with chronic hepatic injury or fatty liver and negative workup for viral hepatitis, drug-induced liver injury, and hemochromatosis (IIB).
- Screening for Wilson's disease in all patients with chronic hepatic injury is not indicated (IIB and IIE).
- Genetic marker testing may be useful in equivocal cases, but testing must be able to detect multiple mutations in the Wilson's disease gene (IIIB).

Autoimmune Hepatitis (AIH)

- Autoimmune hepatitis should be suspected in patients with chronic hepatic injury and increased immunoglobulins and absence of viral markers or risk factors for viral hepatitis (IIIB).
- The diagnosis of type 1 autoimmune hepatitis can be clinically supported by positivity for either anti-nuclear antibody (ANA) or anti-smooth muscle antibody (ASMA) in high titers (IIIB).

Primary Biliary Cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC)

- Primary biliary cirrhosis or primary sclerosing cholangitis should be suspected in patients with chronic cholestasis (IIIB).
- The diagnosis can be clinically supported by positivity for anti-mitochondrial antibody (AMA) (PBC) or anti-neutrophil cytoplasmic antibodies (PSC) in high titers (IIIB).

Alpha1-antitrypsin (A1AT) Deficiency

- Testing for A1AT deficiency may be of benefit in patients with chronic hepatic injury and no other apparent cause, although the role of A1AT deficiency in liver disease in adults is not clearly defined (IIB).
- Testing is especially important in neonates with evidence of hepatic injury (IIB).
- Testing for A1AT variants should be performed by determination of phenotype (IIB).
- Screening patients with chronic hepatic injury for A1AT deficiency is not recommended (IIIB and IIIE).

Other Viruses

Testing for HGV or TTV, in other than a research setting, is not recommended (IIIE).

Monitoring

- In viral hepatitis, viral markers are the most reliable markers of resolution of hepatitis (IIB).
- HCV RNA quantification and genotype are important determinants of duration of combination therapy. To reduce the expense of testing, if feasible, specimens should be obtained before treatment and stored at -70 Â°C pending results of treatment. If this is not possible, testing should be performed before treatment is begun (IIB and IIE).
- In patients with HCV treated with interferon and ribavirin, qualitative HCV RNA should be measured after 24 weeks of treatment to determine potential responders. If genotype and quantitative HCV RNA were not performed but specimens were frozen for their analysis before treatment, those with negative HCV RNA and favorable risk factors should have those tests performed (IB and IE).
- In patients with HCV treated with interferon monotherapy, qualitative HCV RNA and ALT should be measured after 12 weeks of treatment to determine nonresponders (IIB).
- Following treatment in those with negative HCV RNA at 24 weeks, sensitive HCV RNA measurements (currently qualitative assays) should be performed 6 months after the end of treatment to document sustained virologic remission (IIB).
- In untreated patients with HBV, HBeAg should be monitored periodically; once HBeAg is negative and anti-HBe is positive, HBsAg should be monitored periodically to determine viral clearance. With antiviral therapy, HBV DNA should also be used to document viral clearance (IIB).
- In treated patients, a complete blood count with platelets should be measured every week for the first 4 weeks, then monthly thereafter. Thyroid-stimulating hormone should be measured every 3-6 months, or sooner if symptoms of thyroid dysfunction develop. Measurement of ALT should be performed at least monthly (IIIB).
- ALT is the best marker of inflammatory activity available, but it is of limited utility in predicting degree of inflammation and of no use in estimating severity of fibrosis (IIB).

Cirrhosis

- Biopsy is the only definitive marker of progression from chronic hepatitis to cirrhosis (IIB).
- Laboratory markers of fibrosis should not be used except in research studies (IIIB and IIIE).
- Markers of hepatic function that may indicate progression to cirrhosis (AST:ALT ratio, albumin, PT, platelet count) should be measured every 3-6 months in patients with chronic hepatitis (IIIB).

Hepatocellular Carcinoma (HCC)

- Screening for HCC is of questionable benefit in Western populations (IIB and IIE).
- Screening should be confined to high-risk patients (those with severe chronic hepatitis or cirrhosis attributable to alcohol, HBV, HCV, or hemochromatosis) who are candidates for treatment of HCC, if detected (IIIB and IIIE).
- If screening is used, measurement of alpha-fetoprotein (AFP) and ultrasound at intervals no more frequently than every 6 months are recommended (IIB).
- There currently are few data to support the use of other tests (IIIB).

Definitions:

Quality of Evidence

I. Evidence from multiple well-designed randomized controlled clinical trials, each involving a number of patients to be of sufficient statistical power
II. Evidence from at least one large well-designed clinical trial with or without randomization, from cohort or case-controlled analytical studies, or well-designed meta-analysis
III. Evidence based on clinical experience, descriptive studies, or reports of expert committees
IV. Not rated

Strength of the Recommendation

A. Survival benefit
B. Improved diagnosis
C. Improvement in quality of life
D. Relevant pathophysiologic parameters improved
E. Impacts cost of healthcare

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate performance and use of laboratory tests in the evaluation of liver injury

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Total protein is not discussed extensively in this guideline because of its limited utility in evaluation of liver status; its primary utility as a liver-related test is in allowing recognition of increased gamma-globulins, to aid in recognition of patients at increased likelihood of having autoimmune chronic hepatitis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000

GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization
National Academy of Clinical Biochemistry - Professional Association

GUIDELINE DEVELOPER COMMENT

The portion of the guideline dealing with laboratory test performance requirements guidelines was jointly developed with the American Association for the Study of Liver Diseases through their Practice Guidelines Committee.

SOURCE(S) OF FUNDING

Development and publication of these guidelines was supported by grants from Abbot Diagnostics, Diasorin, Inc., Bayer Diagnostics (formerly Chiron Diagnostics), Innogenetics, Inc., and Ortho Clinical Diagnostics.

GUIDELINE COMMITTEE

National Academy of Clinical Biochemistry Committee

American Association for the Study of Liver Diseases Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: D. Robert Dufour, John A. Lott, Frederick S. Nolte, David R. Gretch, Raymond S. Koff, Leonard B. Seeff

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site:

- Word Format
- Portable Document Format (PDF)

Electronic copies are also available in Portable Document Format in Italian and Polish translations of the guideline.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 10, 2003. The information was verified by the guideline developer on June 5, 2003.

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